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Understanding the Structure of High Density Lipoprotein

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Abstract

The high-density lipoprotein (HDL), the carrier of 'good cholesterol', transports cholesterol from periphery cells to liver for catabolism, a process termed reverse cholesterol transport. HDL particles are complexes of amphipathic proteins (e.g. apoA1/apoA2/apoE) with various lipids (phospholipids, cholesterol, cholesterol ester, and triglycerides). Physiologically, it is important to know in detail the structure of HDL so its lipid transport properties can be restored in case of adverse effects. Our approach to solving the structure of HDL is to use a combination of biophysical techniques like small angle neutron scattering, mass spectrometry crosslinking, hydrogen-deuterium exchange mass spectrometry to analyze samples of HDL particles of various sizes. In this project we focused on obtaining and characterizing HDL particles. We expressed the wild-type and N-terminus truncated forms of apoA1, as a regular and deuterated protein in *E. coli*, purified the protein and used it to prepare nHDL particles reconstituted with various lipids (POPC, DMPC, cholesterol). The nHDL preparations obtained are heterogeneous (particles of different sizes). Next we will separate the particles using size-exclusion chromatography and characterize them by employing: electrophoretic gel analysis, light scattering, and lipid composition analysis (to determine the ratio of protein to lipids).